Relevance of Delayed Hospital Admission on Development of Cardiac Rupture During Acute Myocardial Infarction: Study in 225 Patients With Free Wall, Septal or Papillary Muscle Rupture

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Objectives. We analyzed the possible relation between the presence of a hospital admission delay (≥ 24 h), undue physical effort or recurrence of anginal pain, alone or in combination, with the development of free wall rupture (FWR), septal rupture (SR) or papillary muscle rupture (PMR) in patients with an acute myocardial infarction (AMI).

Background. Physical activity as a trigger of FWR in AMI remains controversial, and its contribution to SR or PMR remains unknown. Moreover, the role of ischemia or reinfarction as an additional cause of rupture has not been explored.

Methods. The incidence of hospital admission delay ≥ 24 h with maintenance of some ambulatory activity and the incidence of postinfarction angina were analyzed in consecutive patients with a first AMI with (n = 225) or without rupture (n = 1,012 [control group]) over different time periods.

Results. An admission delay ≥ 24 h occurred in 27 (27.6%) of 98 patients with FWR, 47 (47.0%) of 100 with SR and 14 (51.9%) of 27 with PMR but in only 81 (8%) of 1,012 control patients (p < 0.0001). Information on undue in-hospital effort preceding rupture was available for 111 patients and was present in 17 (32.7%) of 52 with FWR, 9 (18.4%) of 49 with SR and 3 (30%) of 10 with PMR versus only 76 (7.5%) of 1,012 control patients (p < 0.001). Information on postinfarction anginal pain was available for 114 patients with rupture and occurred in 30 (56.6%) of 53 with FWR, 30 (60%) of 50 with SR and 4 (36.4%) of 11 with PMR versus 120 (60%) of 200 control patients (p < 0.0001). Mean age and incidence of male gender, hypertension, absence of heart failure, single-vessel disease or occlusion of the infarct-related artery were comparable among the groups with FWR, SR or PMR.

Conclusions. Delayed hospital admission or undue in-hospital physical activity appears to increase the risk of rupture in patients prone to this complication (i.e., a first transmural AMI, absence of overt heart failure and advanced age); recurrence of ischemia/infarction emerges as a potential additional trigger in a proportion of these patients.
postural changes. In contrast, chest pain was identified as pericarditis when it clearly worsened during respiratory motion and tended to be persistent. Throughout the hospital period, patients were instructed to immediately report any chest pain experienced. Physical activity, such as agitation, repeated vomiting or protracted coughing that necessitated specific medication for their control (e.g., sedatives or anisotropic agents), were considered undue exercise for patients in the acute phase of a myocardial infarction and were recorded. The eventual use of a bed pan for defecation was particularly investigated in patients with rupture but could not be sought reliably in the control group patients. Total CK, CK-MB fraction and glutamic oxaloacetic transaminase were measured every 4 to 6 h during the first 48 to 72 h.

Postmortem examination was performed in 123 patients with rupture (86 with FWR; 28 with SR; 9 with PMR, including 3 who died after mitral valve replacement). Assessment of cardiac tamponade and confirmation of FWR, SR or PMR were carried out, and the cardiac ventricles were sectioned transversely into slices of ~1 cm thick from the apex to 2 to 4 cm caudal to the atrioventricular sulcus. A macroscopic and histologic confirmation of myocardial necrosis was also performed and, in the last 96 patients (17 with SR, 70 with FWR, 9 with PMR), serial cross-sectioning of the main epicardial coronary arteries at 5-mm intervals with gross inspection for maximal lumen narrowing and for presence of an occlusive thrombi was carried out. Coronary angiographic data were available in 79 additional patients (53 with SR, 10 with FWR, and 16 with PMR).

A subset of 1,012 consecutive patients without cardiac rupture with a first transmural AMI, admitted from January 1990 to December 1995, served as a comparison group (control group). The condition of a first transmural AMI, confirmed by coronary angiography was performed in only a fraction of the control group, mainly because of clinical indications (e.g., postinfarction angina, positive stress test results), the corresponding findings are not reported here.

Statistical analysis. A multivariate chi-square test was used to compare categoric variables. Analysis of variance was used for comparison of more than two mean values. The

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<th>Abbreviations and Acronyms</th>
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<tr>
<td>AMI = acute myocardial infarction</td>
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<td>CK = creatine kinase</td>
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<td>ECG = electrocardiogram, electrocardiographic</td>
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<td>FWR = left ventricular free wall rupture</td>
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<td>PMR = papillary muscle rupture</td>
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<td>SR = septal rupture</td>
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### Results

#### Clinical and ECG data (Table 1). Age, male gender and history of arterial hypertension were comparable in patients with FWR, SR or PMR. Hypertension was more often present in the three groups than in the control group, as was diabetes, except for the PMR group. The location of the infarct area was comparable between patients with SR and the control group, whereas the location was less often inferior and more often lateral in patients with FWR than in the SR and control groups (Table 1). As in the control group, all patients with FWR or SR and 23 of those with PMR presented with ST segment elevation, whereas the remaining four patients with PMR presented ST segment depression.

| Admission delay and in-hospital physical effort. A delay of ≥24 h between onset of symptoms and hospital admission occurred in 88 patients with rupture (39.1%), 27 with FWR (27.6%), 47 with SR (47%) and 14 with PMR (51.9%). At least 71 of these patients remained ambulatory at home and did not have continuous bed rest, although the extent of ambulation could not be quantitated. In contrast, a similar delay in admission was observed in only 81 patients in the control group (8%, p < 0.0001). On arrival at the hospital, rupture was present in 48 patients (35.6%), all with delayed admission: 19 with FWR (19.4%), 49 with SR (49%) and 12 with PMR (44.4%). Most patients with in-hospital FWR, SR or PMR were in Killip class I or II on admission (76 [96.2%] of 79 with FWR, 46 [90.2%] of 51 with SR, 13 [86.2%] of 15 with PMR), and the day of rupture was comparable in the three groups (FWR 3.7 ± 4.4, SR 4.1 ± 3.6, PMR 3.7 ± 4.0 days). Of the 79 patients with an in-hospital FWR, 67 (84.8%) died shortly after development of acute tamponade.

Information regarding unusual physical effort before in-

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<th>Table 1. Clinical Data of Patients With a First Transmural Acute Myocardial Infarction With or Without Rupture</th>
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<td>Age (yr)</td>
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<td>Men</td>
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<td>Hypertension</td>
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<td>Diabetes</td>
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<td>AMI site</td>
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<td>Anterior</td>
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* p < 0.0001, † p < 0.001, ‡ p < 0.002, § p < 0.04, versus control group. Data presented are mean value ± SD or number (%) of patients. AMI = acute myocardial infarction; FWR = free wall rupture; PMR = papillary muscle rupture; SR = septal rupture. Student t test was used for comparison of two mean variables with normal distribution and the Mann-Whitney U test for those with abnormal distribution. Results are reported as mean ± SD.
hospital rupture was available for 111 patients: 52 with FWR, 49 with SR and 10 with PMR. Undue effort was documented in 29 patients with rupture (26.1%) (17 with FWR [32.7%], 9 with SR [18.4%], and 3 with PMR [30%]) and in 76 control patients (7.5%, p < 0.0001).

In-hospital chest pain. Information regarding the presence of pericarditic pain during the hospital period was available for 136 patients with in-hospital rupture and for all control patients. Pericarditic pain was present in 43 patients with rupture (31.6%) (27 [37.5%] of 72 with FWR, 13 [26%] of 50 with SR, 3 [21.4%] of 14 with PMR) and in 240 control patients (23.7%) and was thus significantly higher in the subset with FWR than in the control group (p = 0.01). The presence or absence of anginal pain shortly before rupture could be analyzed in 114 (78.6%) of 145 patients with in-hospital rupture and in all control patients. Anginal pain was present in 64 patients with rupture (56.1%): 30 (56.6%) of 53 with FWR, 30 (60%) of 50 with SR and 4 (36.4%) of 11 with PMR. During chest pain a conventional 12-lead ECG could be recorded in 39 (60.9%) of the 64 patients (11 with FWR, 17 with SR, and 11 with PMR) and showed receleration or reappearance of the ST segment in 26 (66.7%) (6 with FWR [55%]), 12 with SR [70.6%], and 8 with PMR [72.7%]). However, although in these patients with an available ECG the proportion of changes was high, documentation could be obtained only for 6 (8%) of 72 patients with FWR, 12 (24%) of 50 with SR and 8 (60%) of 14 with PMR. In contrast, postinfarction angina occurred in 121 control patients (12.0%, p < 0.0001) (Fig. 1), and a 12-lead ECG performed in 112 (92.6%) showed receleration or T wave positivity in 65 (58%). Moreover, among the 80 patients in whom a mechanical complication was already present on admission, 43 (53.8%) had experienced one or more episodes of prolonged chest pain (>30 min) before the AMI (8 [44.4%] of 18 with FWR, 30 [61.2%] of 49 with SR, 5 [41.7%] of 12 with PMR).

Histologic evidence of infarct extension was seen at necropsy in 7 of 28 patients with SR and in 3 of 9 with PMR, all without a previous infarction.

When we analyzed only the 76 patients who experienced rupture during the recruitment interval for the control group (years 1990 to 1995), the proportion with an admission delay >24 h and the frequency of in-hospital undue effort or anginal pain before rupture were comparable to that of patients admitted in the preceding years (Table 2).

**Coronary angiographic/anatomic data.** Although the proportion of patients with one-, two- or three-vessel disease varied somewhat among the three groups (p < 0.05), single-vessel disease had the highest incidence in each group (Fig. 2), and most patients had either one- or two-vessel disease (FWR 96%, SR 90%, PMR 75%). However, the culprit artery differed significantly (p < 0.0001) and was mainly the left circumflex or the left anterior descending coronary artery in the FWR group, the right or the left anterior descending coronary artery in the SR group and the right or the left circumflex coronary artery in the PMR group (Fig. 3). The incidence of total occlusion of the infarction-related artery was high in the three groups (73 [95%] of 77 for FWR, 59 [88%] of 67 for SR, 16 [67%] of 24 for PMR).

**Discussion**

Admission delay and physical strain. One of the relevant findings of our work is the increased incidence of admission delay and physical strain in patients with SR or PMR compared to control patients (Table 2). The high incidence of single-vessel disease in each group is apparent.

![Figure 1](https://example.com/image1)

**Figure 1.** The incidence of postinfarction angina in patients with SR, FWR or PMR was significantly higher than that in control patients with a first transmural AMI without rupture. *p < 0.0001. **p < 0.04.

![Figure 2](https://example.com/image2)

**Figure 2.** Distribution of one-, two- or three-vessel disease (stenosis >70%) in patients with FWR, SR or PMR. The high incidence of single-vessel disease in each group is apparent.

### Table 2. Frequency of Admission Delay (≥24 h), In-Hospital Unusual Physical Effort and Angina in Patients With Rupture (years 1978 to 1989 and 1990 to 1995) and Control Patients

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<tr>
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<th>Control Patients (no rupture)</th>
<th>Patients With Rupture (years 1978 to 1989)</th>
<th>Patients With Rupture (years 1990 to 1995)</th>
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<tbody>
<tr>
<td>Admission delay ≥24 h</td>
<td>81 (8%)</td>
<td>58 (38.9%)</td>
<td>30 (39.5%)</td>
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<tr>
<td>In-hospital angina</td>
<td>120 (11.9%)</td>
<td>28/52 (53.8%)</td>
<td>36/62 (58.1%)</td>
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<tr>
<td>In-hospital unusual</td>
<td>76 (7.5%)</td>
<td>11/50 (22.0%)</td>
<td>17/61 (27.9%)</td>
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<td>physical effort</td>
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Data presented are number (%) of patients.
delay among patients who experienced some form of cardiac rupture. Delayed hospital admission was generally associated with more protracted or recurrent chest pain, the persistence of some physical activity, a delayed diagnosis of AMI and inadequate treatment. Protracted or recurrent chest pain (4,5,8,11,12) as well as persistence of physical activity (1–5) were previously observed to be associated with increased incidence of FWR, particularly in mental institutions (2). Admission delay occurred not only in our patients with FWR but also, and more frequently so, in those with SR or PMR, an observation much less established, most likely because most patients with FWR die before admission to the hospital (19,20). In fact, Jetter and White (2) found a 73% rate of rupture in 22 autopsy cases of AMI in a mental institution and attributed this rate to lack of recognition of AMI and continued patient activity. Likewise, rupture was present on arrival at the hospital in nearly 90% of our patients with an admission delay. Moreover, in an appreciable proportion of patients, undue physical strain also preceded in-hospital cardiac rupture. Undue or unusual effort was also considered in the context of an AMI and was identified as that associated with straining at stool while using a bed pan, persistent disorientation/agitation or protracted vomiting or coughing that required specific medication (e.g., sedatives, antiemetics). Although similar undue effort was much less frequently observed in the control group, it is likely that some of this activity went unreported. Thus, the lack of more accurate information about physical activity in the control patients is a drawback of the study. This limitation notwithstanding, our findings—prospective in more than two-thirds of patients—would lend further support to the role of physical strain as a possible trigger of rupture (2–5). In line with this reasoning we recently reported (21) a low incidence of rupture in patients with a subacute FWR treated with pericardiocentesis, prolonged rest and blood pressure control. Although several investigators have disputed the relevance of physical activity in cardiac rupture, they have often failed to report on the specific activity before rupture (6–8). Moreover, in a number of patients with FWR this information is not available because they die suddenly of tamponade. Because most of these physical efforts implicate a Valsalva maneuver, we speculate that phase 4 (overshoot) is of particular risk because it entails the largest increase in systolic blood pressure, and hence in ventricular wall strain, unopposed by a parallel increase in intrathoracic pressure.

Recurrent chest pain. The second contribution of our study is the recognition that intense chest pain precedes in-hospital rupture in a sizable proportion of patients. Even though persistent chest pain or its recurrence has been acknowledged to be associated with FWR (5,7,8,11,22) and, in fewer reports, with SR (9,23) or PMR (18,24), its potential relevance has not been explored. London and London (7) reported that 26 of their 47 patients with rupture had protacted or new chest pain before rupture (55%), as opposed to 20 of 200 who died of AMI without rupture (10%). Also, in patients who developed FWR after the first 24 h, Rasmussen et al. (8) documented that a new attack of pain frequently commenced the terminal event. Moreover, Kishon et al. (23) reported a 35% incidence of persistent angina in 40 patients with SR, and Barbour and Roberts (18) reported that 21 of their 22 autopsy cases of PMR had died suddenly outside the hospital after 5 to 7 of repeated bouts of chest pain. The possibility that in some patients with FWR, chest pain was in part related to pericardial distension or pericarditis (12) cannot be excluded, but in most patients from the three subsets chest pain preceding rupture was virtually indistinguishable from that during AMI and was not infrequently associated with acute ECG changes in the leads overlying the infarcted area, suggesting that it could be caused by peri-infarction ischemia or reinfarction in at least some patients. Even though previous ECG observations during rupture are scanty and are confined to FWR and to a monitor lead (5,25), they are in line with our findings using a 12-lead ECG. These observations during the acute phase of rupture add to the recently described ECG pattern seen before rupture that includes persistent ST segment elevation (12,26) or lack of evolutionary T wave changes, or both (12). In some instances, particularly in SR and PMR where there was a delay between rupture and death or operation, reinfarction could be confirmed at necropsy. Our contention that reinfarction may be a more frequent cause of rupture, and at a much earlier interval than heretofore suspected (7), may be supported by detailed histologic studies showing that rupture tends to occur in areas of infarction with more recent necrosis (3,27). In contrast, in a number of patients with FWR reinfarction cannot be detected histologically because these patients die shortly after rupture. We speculate that in patients with FWR or SR that follows a recurrence of angina beyond the first 24 h, myocardial ischemia may affect the formerly preserved outer layer of the jeopardized area. The consequent loss of contractile force could facilitate rupture at the point of highest wall strain. In keeping with this possibility, recent experimental studies (28) have indicated that even brief periods of ischemia may cause some collagen loss, thereby weakening the supporting framework of the ischemic zone.

Figure 3. Distribution of the infarct-related artery in patients with FWR, SR or PMR. The most salient findings were the reduced involvement of the left anterior descending coronary artery (LAD) in patients with PMR, the left circumflex coronary artery (CFX) in those with SR and the right coronary artery (RCA) in those with FWR.
Study limitations. The present study was in part retrospective; therefore some information about physical activity before hospital admission was unavailable. However, patients with a delayed hospital admission generally maintained some physical activity at home and often went to seek medical attention, particularly after the pain had partially subsided. Another potential drawback is the reduced number of patients in whom an ECG could be performed during pain preceding FWR, thereby limiting the potential implication of ischemia/reinfarction as a trigger of this complication. One major reason for this limitation is that many of these patients died suddenly of tamponade before an ECG could be recorded. Also, and for the same reason, the nature of the chest pain could not always be determined. Furthermore, objective evidence of myocardial ischemia was only available from the ECG and involved only a small proportion of patients (26% [18%] of 145), although when patients with an available ECG were considered, the proportion with ECG changes was higher. Some of these patients complained of pericarditic pain a few hours or days preceding FWR, but this was a more consistent finding in those few who temporarily survived this event. Nevertheless, the incidence of pericarditic pain in these patients (36%) was lower than that reported by Oliva et al. (12) (86%), probably because these investigators included only “late” FWR in their series (>48 h), which allows for the pericarditis to be manifest, whereas our patients were not selected and more closely represent the early rupture subset, including the 28% who had rupture before admission.

Clinical implications. According to our data, patients who present with cardiac rupture during AMI (either FWR, SR or PMR) share several clinical features, such as a first AMI, age >50 to 55 years, history of arterial hypertension, absence of heart failure before rupture and presence of protracted or recurrent anginal or angina-like pain. An important number of them engaged in sustained physical activity after onset of AMI, particularly before hospital admission. Thus, patients with the aforementioned profile who are admitted late are at increased risk of presenting, in the emergency room, with some form of cardiac rupture. Furthermore, these patients should be cautioned not to undertake any undue physical effort, particularly during the first week, to avoid excessive strain on the infarcted wall, and should undergo strict blood pressure control. Moreover, they should be followed up closely for recurrence of chest pain because this recurrence may lead to some form of rupture. Finally, because rupture ultimately develops in an area subtended by a totally occluded artery, it is likely that early reperfusion and maintenance of an open artery may substantially reduce the incidence of these complications.

References